Summary Minutes of the
U.S. Environmental Protection Agency
Science Advisory Board
Exposure and Human Health Committee and FIFRA SAP liaisons
Meeting
May 30-31, 2012

EHHC members:

Dr. R. Thomas Zoeller, Chair
Dr. Claude Emond
Dr. Anna Fan
Dr. Alfred Franzblau
Dr. Maida Galvez
Dr. Chris Gennings
Dr. Gary Ginsberg
Dr. Robert Goble
Dr. Russ Hauser
Dr. Laurie Haws
Dr. Darryl Hood
Dr. Gloria Post
Dr. Virginia Rauh
Dr. Barry Ryan
Dr. John Vena
Dr. Clifford Weisel
Dr. Robert Wright

FIFRA SAP liaisons:

Dr. Janice Chambers
Dr. Daniel Schlenk

Purpose: To receive briefings from EPA offices and to develop advice for advancing the EPA's application of Computational Toxicology (CompTox) data into the development of EPA hazard and risk assessments.

Designated Federal Officer: Dr. Suhair Shallal, Designated Federal Officer

Other EPA Staff: Vicki Dellarco, Elizabeth Doyle, Robert Kavlock, Tina Bahadori, Jeff Morris, Jennifer Seed, Jim Jones, Ila Cote, Bob Sonawane, Kate Guyton, Kathleen Raffaele, Monica Linnenbrink, Kevin Crofton, Susan Euling, Stan Barone, David Dix

Public: Pat Rizzuto (BNA), Puneet Kollipara (Inside Washington Publ.), Eric Carlson (GE Co.), Rosanne Foley (Dupont), Rick Becker (ACC) Jennifer McPartland (EDF), Richard Denison (EDF), Bruce Fowler (ICF Int.), Steve Risotto (ACC), Nancy Beck (ACC) Cheryl Hogue (C&E News), Chris Knight (Pesticide and Chem Policy), William Mendez (ICF), Pat Casano (GE), Kim Osborn (ICF)

Meeting Materials and Meeting Webpage:
The materials listed below may be found on the meeting webpage at:
http://yosemite.epa.gov/sab/sabproduct.nsf/02ad90b136fc21ef85256eba00436459/5a6494c3001ab046852579580076cad8!OpenDocument

- Agenda
- Federal Register Notice
- Committee Charge
- Roster
- Agency-provided Background Material
  - NCCT background material
  - OCSPP document submitted to SAP May 2011
  - SAP report on OCSPP document August 2011
- Agency Briefing Material
  - Presentation from NCEA by Ila Cote
  - Presentation from OCSPP and OW by Vicki Dellarco
  - Presentation from OCSPP by Jim Jones
  - Presentation from ORD by Robert Kavlock
  - Presentation from the NCCT by David Dix

Meeting Summary

The discussion followed the plan presented in the meeting agenda.

MONDAY, MAY 29, 2012

Dr. Shallal convened the meeting and explained that the Science Advisory Board operates under the Federal Advisory Committee Act. Dr. Vanessa Vu, Director of the SAB Staff Office welcomed everyone and thanked panelists for travelling to the meeting. Dr. Zoeller described the purpose of the meeting as an opportunity to hear from EPA representatives about the CompTox research program and the use of CompTox data in the agency's risk assessments. He then reviewed the agenda and asked everyone to introduce themselves.

Dr. Bob Kavlock, Deputy Assistant Administrator for Science in EPA's Office of Research and Development (ORD), presented an overview of ORD's mission and explained the goals of the computational toxicology research program. Dr. David Dix then followed and presented a more comprehensive description of CompTox research within the agency and its current and future application. He explained the current approach of identifying adverse outcome pathways (AOPs) in determining toxicity of chemicals and how they will be used in decision-making. Dr. Ila Cote explained the NexGen program and its importance in creating "a cheaper, faster and more robust system for chemical risk assessment by incorporating new knowledge about system biology". She talked about the various initiatives undertaken to bring the new technologies into the risk assessment process.

The meeting reconvened after lunch; Mr. Jim Jones, Acting Assistant Administrator for the Office of Chemical Safety & Pollution Prevention, told the committee about the importance of

the CompTox program and its role in enhancing risk assessment and addressing programmatic needs. He explained that with the large number of chemicals that have to be assessed, new methodologies had to be developed. He also stated that there are a number of applications where CompTox research may be helpful, including, prioritizing, categorizing and screening chemicals. The committee also heard from representatives of the Office of Pesticide Programs, Office of Water and Office of Chemical Safety & Pollution Prevention, Drs. Dellarco, Doyle and Morris, respectively. In their joint presentation, they explained their respective programmatic needs and the role of CompTox in addressing those needs. They also described the challenges they face in producing credible risk assessments for a huge number of chemicals to meet their regulatory requirements. They described their interaction with ORD scientists to determine the type of information they need for the prioritization and categorization of chemicals. They stated that high throughput assays would assist in saving time and resources by determining the most toxic chemicals which require more comprehensive assessments.

EPA representatives reminded the committee that program offices are expected to make decisions regarding chemicals with or without the use of CompTox information (~2000 chemical submissions per year). Variations of CompTox data are currently being use in the decision-making process including, EpiSuite, QSAR, etc. in addition to physio-chemical properties of chemicals. The agency has also engaged the public, stakeholders and the scientific community to ensure that CompTox information is being used prudently. The FIFRA Scientific Advisory Panel (liaison members are included in this committee) have previously reviewed OCSPP's document entitled, "Integrated Approaches to Testing and Assessment Strategy: Use of New Computational and Molecular Tools". The agency's Pesticide Program Dialogue Committee (PPDC) also commented on the use of CompTox information in risk assessment. They endorsed the use of CompTox and suggested an incremental approach and requested a safety net to make sure toxic chemicals do not fall through the cracks.

Committee members asked questions concerning the type of data being generated through the CompTox research program. Members express concern about the need for a set of criteria and guidance for the use of CompTox data for various applications. Committee members also noted that the integration of exposure data was limited and the agency should do more research on this issue.

A discussion of the challenges the agency faces then ensued. The committee members learned that the chemicals being tested in the ToxCast program were selected based on a collaborative effort with agency program offices. Some of the chemicals selected for use in the ToxCast assays were data-rich, others were data-poor. Currently chemicals on the Chemical Contaminants List (CCL) are selected based on studies in the scientific literature; CompTox research will determine if they will have similar findings. The agency is also creating DASHBOARDS, databases for sharing information.

EHHC members observed that transparency and communication are critical to the successful implementation of CompTox in risk assessment. Training for staff is also important. Partial information on AOPs should also be used to support decisions and in prioritizing of chemicals. Incrementally replacing traditionally used apical endpoints with new information is a good idea.

TUESDAY MAY 31, 2012

The meeting was re-convened at 8:30 am. Dr. Zoeller opened the meeting with a brief summary of the previous day's discussion. He then invited the one registered public speaker, Dr. Richard Becker of ACC, to present his comments. Dr. Becker stated that the discussion of the EHHC on the use of CompTox in EPA risk assessment was timely. Significant advances have been made and it was important to discuss how this information was going to be used. He stated that the interpretation and use of prediction models should be determined.

The committee members then each discussed their impressions of the agency's presentations. Dr. Chambers, a FIFRA SAP liaison member, recounted that the SAP was enthusiastic about the use of CompTox but was concerned about the biological plausibility of AOPs. Dr. Weisel was concerned that exposure information was not being included. He suggested that the difference between concentration versus exposure needed to be clarified.

Committee members suggested that a guide on how to use the data should be prepared. Data quality should be monitored and positive and negative controls should be standardized. Some suggested that the technology that is being used has been shown to be reliable. The data is being made publically available as a way to ensure quality. Committee members also noted that metabolism of chemicals is another area of concern.

For epidemiologists, Dr. Hauser said, the focus is on outcomes and not the AOPs. Their concern is how will *in vitro* AOPs map to health outcomes? The use of biomarkers, he suggested may help to inform which assays to develop or use. Agency representatives reminded the committee that CompTox is only one tool amongst many, and that decisions are currently being made based on available data. Dr. Ryan added that CompTox also has associated uncertainty which should be considered.

Committee members agreed that the current CompTox research is responsive to the need for screening chemicals; however, dose/response assessments are not yet feasible. Committee members suggested that using the Deep Water Horizon (DWH) incident as a case study may be helpful. Quantifying the uncertainties and limitations of the data is important and should be presented in a transparent manner. A guidance document for how and when to use certain types of data is essential.

Dr. Zoeller stated that the discussion has been very informative and asked committee members if they needed more information in order to address the charge questions. The committee requested additional information from the agency representatives, including: an outline of program office needs, ORD's DWH fact sheet and paper, information on exposure research (webinar on ExpoCast).

Dr. Shallal suggested that committee members re-visit the CompTox webpage in order to learn more about ORD's current research initiatives. Dr. Zoeller asked committee members to address the charge questions and send their preliminary comments and requests for additional information to Dr. Shallal by June 11, 2012. A preliminary draft report along with the requested information would be sent to committee members within 3 weeks. Dr. Shallal informed committee members that she would send a detailed timeline explaining the steps in the report

writing process after the meeting. Before adjourning, she also reminded members to cc: her on any correspondence with others regarding the subject matter under review. She also asked committee members to address any questions or concerns to her and she would forward the information to the appropriate individual(s).

On Behalf of the Committee,
Respectfully Submitted,

/s/
Suhair Shallal, Ph.D.
Designated Federal Officer

Certified as Accurate:

/s/
R. Thomas Zoeller, Ph.D.
Chair, SAB Exposure and Human Health Committee

NOTE AND DISCLAIMER: The minutes of this public meeting reflect diverse ideas and suggestions offered by committee members during the course of deliberations within the meeting. Such ideas, suggestions, and deliberations do not necessarily reflect definitive consensus advice from the panel members. The reader is cautioned to not rely on the minutes to represent final, approved, consensus advice and recommendations offered to the Agency. Such advice and recommendations may be found in the final advisories, commentaries, letters, or reports prepared and transmitted to the EPA Administrator following the public meetings